UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,341	11/08/2004	Luet Lok Wong	480821.00008	5914

26710 7590 01/06/2009

QUARLES & BRADY LLP
411 E. WISCONSIN AVENUE
SUITE 2040
MILWAUKEE, WI 53202-4497

EXAMINER	
DAM, DUSTIN Q	
ART UNIT	PAPER NUMBER
1795	

MAIL DATE	DELIVERY MODE
01/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,341	WONG ET AL.	
	Examiner	Art Unit	
	DUSTIN Q. DAM	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4 and 6-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4 and 6-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. This Office Action is in response to the Amendments to the Claims/Specification, Remarks, and Declaration filed October 22, 2008.

2. In view of the Amendments to the Claims filed October 22, 2008, the rejections of claims 1-16 under 35 U.S.C. 102(b) and 103(a) previously presented in the Office Action sent April 29, 2008 have been withdrawn.

3. In view of the Amendments to the Specification, the objection to the specification previously presented in the Office Action sent April 29, 2008 is withdrawn.

4. Claims 3, 4, and 6-19 are currently pending and have been fully considered.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 3, 4, 6, 13, and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over COSNIER et al. ("*An Original Electroenzymatic System: Flavin Reductase-Riboflavin for the Improvement of Dehydrogenase-Based Biosensors. Application to the Amperometric Detection of Lactate* " Electroanalysis Vol. 9 No. 9 (1997) pages 685-688) in view of IKEDA et al. (U.S. Patent 5,575,895).

a. With regards to claim 15, COSNIER et al. discloses an electrochemical cell comprising a sample holding means (FIG. 2 "Polymer"), a solution comprising a dehydrogenase enzyme (FIG. 2 "dehydrogenase") structurally capable of converting an analyte substrate to its product, NAD^+ or $NADP^+$ (FIG. 2 "$NAD(P)^+$"), a NADH or NADPH reductase (FIG. 2 "flavin reductase") and a redox active agent (FIG. 2 "riboflavin"), and means for detecting and/or quantifying any current generated (FIG. 2 "electrode" & see **2.3 Electrochemical Measurements**, page 686 "Tacussel PRG-DEL potentiostat in conjunction with a Kipp and Zonen BD 91 XY/t recorder").

COSNIER et al. does not appear to explicitly disclose an electrochemical cell wherein the solution comprising the dehydrogenase enzyme, reductase, and redox agent further comprises a buffer. The only difference between the invention, as claimed in claim 15, and the immobilized electrode cell design of COSNIER et al., is the addition of a buffer.

However, IKEDA et al. discloses immobilizing reagents on an electrode surface in a biosensor application comprising a dehydrogenase enzyme (EXAMPLE 1, column 5) which comprises the addition of a buffer (line 26, column 5 "phosphoric acid-citric acid

buffer solution"). The buffer solution functions to maintain a predetermined pH of the immobilized reagents. Although IKEDA et al. and COSNIER et al. are sensing different biological components, both are concerned with immobilizing the reactive reagents on the surface of the working electrode for oxidation/reduction type electrochemical sensing. Maintaining the pH of the immobilized reagents, as disclosed by IKEDA et al. via a buffer, is not exclusively limited to the application disclosed by IKEDA et al. and would offer the same effect for other reagent immobilized electrodes.

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the electrochemical cell of COSNIER et al., to include the addition of a buffer, as disclosed by IKEDA et al., because it would provide for maintaining a predetermined pH of the immobilized reagents on the electrode.

b. With regards to claim 16, COSNIER et al. discloses an electrochemical cell which can be used to carry out a method for monitoring the activity of a redox enzyme in a sample which the enzyme is a dehydrogenase enzyme which uses NAD^+ or $NADP^+$ as a co-factor (FIG. 2) by providing a solution comprising said sample and said dehydrogenase enzyme (FIG. 2 "dehydrogenase"), NAD^+ or $NADP^+$ (FIG. 2 "$NAD(P)^+$"), a NADH or NADPH reductase (FIG. 2 "flavin reductase") and a redox active agent (FIG. 2 "riboflavin"), and measuring the quantity of reduced redox active agent produced by the reductase by electrochemical means wherein electron transfer between the redox active agent and an electrode is correlated to the activity of the redox enzyme or the amount of the substrate (FIG. 2 & see 3rd paragraph of **3. Results and Discussion**, page 687), wherein the electrochemical cell comprises a sample holding

means (FIG. 2 "Polymer"), a solution comprising a dehydrogenase enzyme (FIG. 2 "dehydrogenase") structurally capable of converting an analyte substrate to its product, NAD^+ or $NADP^+$ (FIG. 2 "$NAD(P)^+$"), a NADH or NADPH reductase (FIG. 2 "flavin reductase") and a redox active agent (FIG. 2 "riboflavin"), and means for detecting and/or quantifying any current generated (FIG. 2 "electrode" & see **2.3 Electrochemical Measurements**, page 686 "Tacussel PRG-DEL potentiostat in conjunction with a Kipp and Zonen BD 91 XY/t recorder").

COSNIER et al. does not appear to explicitly disclose an electrochemical cell wherein the solution comprising the dehydrogenase enzyme, reductase, and redox agent further comprises a buffer. The only difference between the invention, as claimed in claim 16, and the immobilized electrode cell design of COSNIER et al., is the addition of a buffer.

However, IKEDA et al. discloses immobilizing reagents on an electrode surface in a biosensor application comprising a dehydrogenase enzyme (EXAMPLE 1, column 5) which comprises the addition of a buffer (line 26, column 5 "phosphoric acid-citric acid buffer solution"). The buffer solution functions to maintain a predetermined pH of the immobilized reagents. Although IKEDA et al. and COSNIER et al. are sensing different biological components, both are concerned with immobilizing the reactive reagents on the surface of the working electrode for oxidation/reduction type electrochemical sensing. Maintaining the pH of the immobilized reagents, as disclosed by IKEDA et al. via a buffer, is not exclusively limited to the application disclosed by IKEDA et al. and would offer the same effect for other reagent immobilized electrodes.

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the electrochemical cell of COSNIER et al., to include the addition of a buffer, as disclosed by IKEDA et al., because it would provide for maintaining a predetermined pH of the immobilized reagents on the electrode.

c. With regards to claim 17, COSNIER et al. discloses a method for monitoring the activity of a redox enzyme in a sample, which enzyme is a dehydrogenase enzyme which uses NAD+ or NADP+ as a co-factor by providing a solution comprising said sample and said dehydrogenase enzyme (FIG. 2 "dehydrogenase"), NAD^+ or $NADP^+$ (FIG. 2 "$NAD(P)^+$"), a NADH or NADPH reductase (FIG. 2 "flavin reductase") and a redox active agent (FIG. 2 "riboflavin") and measuring the quantity of reduced redox active agent produced by the reductase by electrochemical means wherein electron transfer between the redox active agent and an electrode is correlated to the activity of the redox enzyme or the amount of the substrate (FIG. 2 & see 3rd paragraph of **3. Results and Discussion**, page 687).

COSNIER et al. does not appear to explicitly disclose an electrochemical cell wherein the solution comprising the dehydrogenase enzyme, reductase, and redox agent further comprises a buffer. The only difference between the invention, as claimed in claim 17, and the immobilized electrode cell design of COSNIER et al., is the addition of a buffer.

However, IKEDA et al. discloses immobilizing reagents on an electrode surface in a biosensor application comprising a dehydrogenase enzyme (EXAMPLE 1, column 5) which comprises the addition of a buffer (line 26, column 5 "phosphoric acid-citric acid

buffer solution"). The buffer solution functions to maintain a predetermined pH of the immobilized reagents. Although IKEDA et al. and COSNIER et al. are sensing different biological components, both are concerned with immobilizing the reactive reagents on the surface of the working electrode for oxidation/reduction type electrochemical sensing. Maintaining the pH of the immobilized reagents, as disclosed by IKEDA et al. via a buffer, is not exclusively limited to the application disclosed by IKEDA et al. and would offer the same effect for other reagent immobilized electrodes.

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the electrochemical cell of COSNIER et al., to include the addition of a buffer, as disclosed by IKEDA et al., because it would provide for maintaining a predetermined pH of the immobilized reagents on the electrode.

d. With regards to claim 3, independent claim 17 is obvious over COSNIER et al. in view of IKEDA et al. under 35 U.S.C. 103(a) as discussed above. The combination of COSNIER et al. and IKEDA et al. discloses a method wherein NADH or NADPH are produced by the reduction of NAD^+ or $NADP^+$ (COSNIER et al.: FIG. 2) by a redox enzyme (COSNIER et al.: FIG. 2 "dehydrogenase") which concomitantly oxidizes a substrate (COSNIER et al.: 3rd paragraph of **3. Results and Discussion**, page 687).

e. With regards to claim 4, independent claim 17 is obvious over COSNIER et al. in view of IKEDA et al. under 35 U.S.C. 103(a) as discussed above. The combination of COSNIER et al. and IKEDA et al. discloses a method wherein the amount of NADH or NADPH formed is proportional to the amount of the redox enzyme present or the amount of its substrate and hence allows the detection, or quantification, of the enzyme or

substrate in the sample (COSNIER et al.: FIG. 2 & see 3rd paragraph of **3. Results and Discussion**, page 687).

f. With regards to claim 6, independent claim 17 is obvious over COSNIER et al. in view of IKEDA et al. under 35 U.S.C. 103(a) as discussed above. The combination of COSNIER et al. and IKEDA et al. discloses a method wherein the reductase is capable of accepting two electrons from NADH or NADPH (COSNIER et al.: 1st paragraph of **3. Results and Discussion**, page 686 "flavin oxidoreductase "Fre") is capable of accepting two electrons from NADH or NADPH & also see FIG. 2 and 1st paragraph of **3. Results and Discussion**, page 686 discloses "two-electron transfer from reduced pyridine nucleotides").

g. With regards to claim 13, independent claim 17 is obvious over COSNIER et al. in view of IKEDA et al. under 35 U.S.C. 103(a) as discussed above. The combination of COSNIER et al. and IKEDA et al. discloses a method which allows (the term "allows" is interpreted to mean, but not limited to, "capable of") a monitoring of the amount of the substrate, enzyme, NADH or NADPH over time (COSNIER et al.: **2.4 Assays** "time dependent").

h. With regards to claim 18, COSNIER et al. discloses an electrochemical cell comprising a sample holding means (FIG. 2 "Polymer"), a mixture comprising a dehydrogenase enzyme (FIG. 2 "dehydrogenase") structurally capable of converting an analyte substrate to its product, NAD^+ or $NADP^+$ (FIG. 2 "$NAD(P)^+$"), a NADH or NADPH reductase (FIG. 2 "flavin reductase") and a redox active agent (FIG. 2 "riboflavin") which is dried (**2.2 Enzyme Electrode Preperation** "water removed under

reduced pressure"), and means for detecting and/or quantifying any current generated (FIG. 2 "electrode" & see **2.3 Electrochemical Measurements**, page 686 "Tacussel PRG-DEL potentiostat in conjunction with a Kipp and Zonen BD 91 XY/t recorder").

COSNIER et al. does not appear to explicitly disclose an electrochemical cell wherein the solution comprising the dehydrogenase enzyme, reductase, and redox agent further comprises a buffer. The only difference between the invention, as claimed in claim 15, and the immobilized electrode cell design of COSNIER et al., is the addition of a buffer.

However, IKEDA et al. discloses immobilizing reagents on an electrode surface in a biosensor application comprising a dehydrogenase enzyme (EXAMPLE 1, column 5) which comprises the addition of a buffer (line 26, column 5 "phosphoric acid-citric acid buffer solution") which is then dried (line 28-29, column 5). The buffer solution functions to maintain a predetermined pH of the immobilized reagents. Although IKEDA et al. and COSNIER et al. are sensing different biological components, both are concerned with immobilizing the reactive reagents dried on the surface of the working electrode for oxidation/reduction type electrochemical sensing. Maintaining the pH of the immobilized reagents, as disclosed by IKEDA et al. via a buffer, is not exclusively limited to the application disclosed by IKEDA et al. and would offer the same effect for other reagent immobilized electrodes.

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the electrochemical cell of COSNIER et al., to include

the addition of a buffer, as disclosed by IKEDA et al., because it would provide for maintaining a predetermined pH of the immobilized reagents on the electrode.

i. With regards to claim 19, COSNIER et al. discloses an electrochemical cell which can be used to carry out a method for monitoring the activity of a redox enzyme in a sample which the enzyme is a dehydrogenase enzyme which uses NAD^+ or $NADP^+$ as a co-factor (FIG. 2) by providing a mixture comprising said sample and said dehydrogenase enzyme (FIG. 2 "dehydrogenase"), NAD^+ or $NADP^+$ (FIG. 2 "$NAD(P)^+$"), a NADH or NADPH reductase (FIG. 2 "flavin reductase") and a redox active agent (FIG. 2 "riboflavin") which is dried (**2.2 Enzyme Electrode Preperation** "water removed under reduced pressure"), and measuring the quantity of reduced redox active agent produced by the reductase by electrochemical means wherein electron transfer between the redox active agent and an electrode is correlated to the activity of the redox enzyme or the amount of the substrate (FIG. 2 & see 3rd paragraph of **3. Results and Discussion**, page 687), wherein the electrochemical cell comprises a sample holding means (FIG. 2 "Polymer"), a solution comprising a dehydrogenase enzyme (FIG. 2 "dehydrogenase") structurally capable of converting an analyte substrate to its product, NAD^+ or $NADP^+$ (FIG. 2 "$NAD(P)^+$"), a NADH or NADPH reductase (FIG. 2 "flavin reductase") and a redox active agent (FIG. 2 "riboflavin"), and means for detecting and/or quantifying any current generated (FIG. 2 "electrode" & see **2.3 Electrochemical Measurements**, page 686 "Tacussel PRG-DEL potentiostat in conjunction with a Kipp and Zonen BD 91 XY/t recorder").

COSNIER et al. does not appear to explicitly disclose an electrochemical cell wherein the solution comprising the dehydrogenase enzyme, reductase, and redox agent further comprises a buffer. The only difference between the invention, as claimed in claim 16, and the immobilized electrode cell design of COSNIER et al., is the addition of a buffer.

However, IKEDA et al. discloses immobilizing reagents on an electrode surface in a biosensor application comprising a dehydrogenase enzyme (EXAMPLE 1, column 5) which comprises the addition of a buffer (line 26, column 5 "phosphoric acid-citric acid buffer solution") which is then dried (line 28-29, column 5). The buffer solution functions to maintain a predetermined pH of the immobilized reagents. Although IKEDA et al. and COSNIER et al. are sensing different biological components, both are concerned with immobilizing the reactive reagents dried on the surface of the working electrode for oxidation/reduction type electrochemical sensing. Maintaining the pH of the immobilized reagents, as disclosed by IKEDA et al. via a buffer, is not exclusively limited to the application disclosed by IKEDA et al. and would offer the same effect for other reagent immobilized electrodes.

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the electrochemical cell of COSNIER et al., to include the addition of a buffer, as disclosed by IKEDA et al., because it would provide for maintaining a predetermined pH of the immobilized reagents on the electrode.

8. Claims 7, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over COSNIER et al. ("*An Original Electroenzymatic System: Flavin Reductase-Riboflavin for the*

Improvement of Dehydrogenase-Based Biosensors. Application to the Amperometric Detection of Lactate " Electroanalysis Vol. 9 No. 9 (1997) pages 685-688) in view of IKEDA et al. (U.S. Patent 5,575,895), as applied to claims 3, 4, 6, 13, and 15-19, and in further view of WONG et al. (U.S. Patent 6,117,661).

a. With regards to claims 7, 9, and 10, independent claim 17 is obvious over COSNIER et al. in view of IKEDA et al. under 35 U.S.C. 103(a) as discussed above. The combination of COSNIER et al. and IKEDA et al. disclose method for detecting the presence, absences, or concentration of NADH or NADPH in a sample comprising a reduction/oxidation sequence with a redox enzyme, reductase, and active redox agent. COSNIER et al. discloses a method wherein the reductase allows transfer of electrons to/from the NADH or NADPH and the redox active agent (COSNIER et al.: FIG. 2 "flavin reductase").

The combination of COSNIER et al. and IKEDA et al. does not appear to explicitly disclose a method wherein the reductase, which allows two-electron transfer between the NADH/NADPH and the redox active agent, is specific to NADH and is a putidaredoxin reductase of the cytochrome $P450_{cam}$ enzyme system from pseudonomas putida.

However, WONG et al. discloses a composition to be a cytochrome $P450_{cam}$ from Pseudonomas putida (line 19-21, column 1). WONG et al. discloses the study of putidaredoxin reductase comprising the $P450_{cam}$ in an oxidation reaction with NADH as a co-factor (line 34-38, column 3). WONG et al. also discloses the reductase comprising the $P450_{cam}$ shows much higher turnover activities (line 43-45, column 3).

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the method, as disclosed by the combination of COSNIER et al. and IKEDA et al., to include using putidaredoxin reductase comprising the $P450_{cam}$ which is specific to NADH, as disclosed by WONG et al., because WONG et al. suggest the application of the reductase in an oxidation reaction with NADH, because one with ordinary skill would have predicted success in the substitution of the putidaredoxin reductase comprising the $P450_{cam}$ in the method disclosed by the combination of COSNIER et al. and IKEDA et al. based on the known properties shown by WONG et al. of the reductase in an oxidation reaction with NADH, and because the reductase, as disclosed by WONG et al., in combination with NADH yields higher turnover activities.

9. Claims 7, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over COSNIER et al. ("*An Original Electroenzymatic System: Flavin Reductase-Riboflavin for the Improvement of Dehydrogenase-Based Biosensors. Application to the Amperometric Detection of Lactate* " Electroanalysis Vol. 9 No. 9 (1997) pages 685-688) in view of IKEDA et al. (U.S. Patent 5,575,895), as applied to claims 3, 4, 6, 13, and 15-19, and in further view of FREDRICKS et al. (*"Stimulation of the Transhydrogenase Activity of Spinach Ferredoxin-Nicotinamide Adenine Dinucleotide Phosphate Reductase by Ferredoxin*" The Journal of Biological Chemistry Vol. 246 No. 5 (1971) pages 1201-1205).

a. With regards to claims 7, 11, and 12, independent claim 17 is obvious over COSNIER et al. in view of IKEDA et al. under 35 U.S.C. 103(a) as discussed above. The combination of COSNIER et al. and IKEDA et al. disclose method for detecting the

presence, absences, or concentration of NADH or NADPH in a sample comprising a reduction/oxidation sequence with a redox enzyme, reductase, and active redox agent. COSNIER et al. discloses a method wherein the reductase allows transfer of electrons to/from the NADH or NADPH and the redox active agent (COSNIER et al.: FIG. 2 "flavin reductase").

The combination of COSNIER et al. and IKEDA et al. does not appear to explicitly disclose a method wherein the reductase, which allows two-electron transfer between the NADH/NADPH and the redox active agent, is specific to NADPH and is spinach ferrodoxin reductase.

However, FREDRICKS et al. discloses a study of spinach ferrodoxin reductase with NADPH (1st paragraph, **SUMMARY**). As made evident by FREDRICKS et al., the application of spinach ferrodoxin reductase specified for NADPH is a conventional and known technique.

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the method, as disclosed by the combination of COSNIER et al. and IKEDA et al., to include using spinach ferrodoxin reductase with NADPH as the reductase, as disclosed by FREDRICKS et al., because the application of spinach ferrodoxin is a conventional technique that one with ordinary skill would have predicted success in the substitution of the reductase disclosed by FREDRICKS et al. in the method disclosed by the combination of COSNIER et al. and IKEDA et al. based on the known properties of spinach ferrodoxin reductase specified for NADPH.

10. Claims 8 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over COSNIER et al. ("*An Original Electroenzymatic System: Flavin Reductase-Riboflavin for the Improvement of Dehydrogenase-Based Biosensors. Application to the Amperometric Detection of Lactate* " Electroanalysis Vol. 9 No. 9 (1997) pages 685-688) in view of IKEDA et al. (U.S. Patent 5,575,895), as applied to claims 3, 4, 6, 13, and 15-19, and in further view of BU et al. ("*NAD(P)H Sensor Based on Enzyme Entrapment in Ferrocene-Containing Polycrylamide-Based Redox Gels*" Anal. Chem. Vol. 70 No. 20 (1998) pages 4320-4325).

a. With regards to claims 8 and 14, independent claim 17 is obvious over COSNIER et al. in view of IKEDA et al. under 35 U.S.C. 103(a) as discussed above. The combination of COSNIER et al. and IKEDA et al. disclose method for detecting the presence, absences, or concentration of NADH or NADPH in a sample comprising a reduction/oxidation sequence with a redox enzyme, reductase, and active redox agent. COSNIER et al. discloses a method wherein the redox active agent accepts two-electrons from the reductase to transfer to the electrode (FIG. 2 "riboflavin").

The combination of COSNIER et al. and IKEDA et al. does not appear to explicitly disclose a method wherein the redox active agent is ferricyanide ($Fe(CN)_6^{3-}$), which is not an organic dye.

However, BU et al. discloses a method for detecting NADH and NADPH and discloses a redox active agent for accepting two-electrons from a reductase to generate a current in an electrode (equation (1) & (2) of the 1st column, page 4321). BU et al. discloses known redox active agents can be ferricyanide (1st column, page 4321 after equations (1) & (2) "ferricyanide").

Thus, at the time of the invention, it would have been obvious to a person having ordinary skill in the art to modify the method, as disclosed by the combination of COSNIER et al. and IKEDA et al., to include using ferricyanide as the redox active agent for accepting two-electrons from the reductase to transfer to the electrode, as disclosed by BU et al., because ferricyanide is a conventional redox active agent in an application to detect NADH and NADPH as made evident by BU et al. and because one with ordinary skill would have predicted success in the substitution of ferricyanide as the redox active agent in the method disclosed by the combination of COSNIER et al. and IKEDA et al.

Response to Arguments

11. Applicant's arguments with respect to claims 1-16 presented in the Remarks and Declaration filed October 22, 2008 have been considered but are moot in view of the new ground(s) of rejection.

a. Applicant's amendments including newly added limitations regarding the addition of a buffer has obviated the previous 102(b) rejections of the claims. However, the newly combined references including IKEDA et al. is believed to read on the claimed "buffer" limitation in an immobilized reagent electrode application.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DUSTIN Q. DAM whose telephone number is (571)270-5120. The examiner can normally be reached on Monday through Thursday, 7:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on (571)272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kaj K Olsen/
Primary Examiner, Art Unit 1795

dd
January 2, 2009